

**REMARKS**

In the Office Action, claims 4 and 9-14 were objected to under 37 CFR 1.75 as substantial duplicates of claims 38 and 42-47. Claim 6 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1, 2, 6-8 and 16 were rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 5,849,497 ("Steinman") in view of Orum et al., Nucleic Acids Research 21:5332 ("Orum"). Claims 3, 4, 9-12, 38-45 and 49 were rejected under 35 U.S.C. § 103(a) over Steinman and Orum in view of U.S. Patent No. 5,863,717 ("Lancaster"). Claims 13, 15, 46 and 48 were rejected under 35 U.S.C. § 103(a) over Steinman and Orum in view of U.S. Patent No. 6,045,993 ("Mahony"). Claims 14 and 47 were objected to as duplicates and as dependent on rejected base claims but were otherwise allowable.

In response to the Office Action, claims 1-16 have been cancelled, and claims 50-73 have been added. Support for the new claims may be found throughout the application as filed, for example in claims 1-16, 22 and 24 as filed. Claim 72 finds support at least at page 10 lines 23-28. Claim 73 finds support at least at page 10 lines 14-15. Claim 74 finds support at least in claims 1 and 14 as filed. No new matter is added.

The cancellation of claims 1-16 renders moot the objection under 37 CFR 1.75, and the rejection of claim 6 under 35 U.S.C. § 112, second paragraph

**The rejection under 35 USC 103(a) over Steinman in view of Orum**

Claims 1, 2, 6-8 and 16 were rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 5,849,497 ("Steinman") in view of Orum et al., Nucleic Acids Research 21:5332 ("Orum"). This rejection is moot, as claims 1-16 have been cancelled.

**The rejection under 35 USC 103(a) over Steinman and Orum in view of Lancaster**

Claims 3, 4, 9-12, 38-45 and 49 were rejected under 35 U.S.C. § 103(a) over Steinman and Orum in view of U.S. Patent No. 5,863,717 ("Lancaster"). The rejection of claims 3, 4, 9-12 and 38-45 is rendered moot by their cancellation. The rejection of claims 38-45 and 49 is traversed.

Steinman teaches the use of non-extendable oligonucleotides having phosphodiester linkages to block PCR amplification using a polymerase lacking 5' exonuclease activity.

Steinman specifically teaches away from using the PNA molecules of Orum, which are said to be not easily synthesized, not readily available, and expensive. *See* col. 2 lines 56-65, col. 3 line 64-col. 4 line 5, and claim 1. Steinman does not teach or suggest amplification of HPV, the subregions thereof recited in the claims, or the specific sequences recited in the claims.

Orum describes the use of PNA molecules to block PCR amplification. Orum does not teach or suggest HPV, the subregions thereof recited in the claims, or the specific sequences recited in the claims.

Lancaster teaches the amplification of multiple strains of HPV using universal primers specific for the E1 region thereof, and the distinction between the strains by hybridization using type specific probes. Lancaster also teaches the detection of whether any product is produced by the amplification reaction using gel electrophoresis, but does not teach or suggest how to do this in a strain specific manner. Lancaster does not teach or suggest the amplification of any other regions of HPV, nor the selective amplification of any strains. Lancaster teaches that his method is perfectly adequate for distinguishing which HPV strains are present in a sample.

A new combination of elements can be patented “whether it be composed of elements all new, partly new or all old.” *Rosmount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1546, 221 USPQ 1, 7 (CAFC 1984). The Court of Appeals for the Federal Circuit has forcefully stated that a claim rejection must provide a specific motivation in the art for combining elements from cited art in order to establish obviousness of a new combination.

“[C]ase law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. ... Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability--the essence of hindsight. ... [Evidence of a suggestion, teaching, or motivation to combine] must be clear and particular. ... Broad conclusory statements regarding the teaching of multiple references, standing alone, are not ‘evidence.’ ... [A] reference-by-reference, limitation-by-limitation analysis fails to demonstrate how the [cited] references teach or suggest their combination ... to yield the claimed invention,” and a conclusion of obviousness based on such an analysis “as a matter of law, cannot stand.” *In re Dembiczak*, 175 F.3d 994, 999, 1000, 50 USPQ2d 1614, 1617, 1618 (Fed. Cir. 1999), emphasis added.

*Dembiczak* involved patent claims to "a large trash bag made of orange plastic and decorated with lines and facial features, allowing the bag, when filled with trash or leaves, to resemble a Halloween-style pumpkin, or jack-o'-lantern." *Dembiczak*, 175 F.3d at 996, 50 USPQ2d at 1616. The prior art cited by the Board included: a book describing how to teach children to make a "Crepe Paper Jack-O-Lantern;" a book describing a method of making a "paper bag pumpkin" by stuffing a bag with newspapers, painting it orange, and then painting on facial features with black paint; a U.S. Patent describing a bag apparatus wherein the bag closure is accomplished by the use of folds or gussets in the bag material; design patents issued to *Dembiczak*; and prior art "conventional" plastic lawn or trash bags. The Federal Circuit held that the claimed pumpkin-style trash bag was not obvious because there was no clear, particular motivation to combine the cited references.

This holding of *Dembiczak* that evidence of motivation to combine must be clear and particular to establish obviousness has been emphasized over and over again by the Federal Circuit since *Dembiczak* was decided. It was strongly reemphasized in *Ruiz v. A.B. Chance Co.*, 57 USPQ2d 1161 (Fed. Cir. 2000):

In order to prevent a hindsight-based obviousness analysis, we have clearly established that the relevant inquiry for determining the scope and content of the prior art is whether there is a reason, suggestion, or motivation in the prior art or elsewhere that would have led one of ordinary skill in the art to combine the references. See, e.g., *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("[T]he Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."); *In re Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617 ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."). "Determining whether there is a suggestion or motivation to modify a prior art reference is one aspect of determining the scope and content of the prior art, a fact question subsidiary to the ultimate conclusion of obviousness." *Sibia Neurosciences, Inc. v. Cadus Pharma. Corp.*, 225 F.3d 1349, 1356, 55 USPQ2d 1927, 1931 (Fed. Cir. 2000); *Tec Air, Inc. v. Denso Mfg., Inc.*, 192 F.3d 1353, 1359, 52 USPQ2d 1294, 1298 (Fed. Cir. 1999) (stating that the factual underpinnings of obviousness include whether a reference provides a motivation to combine its teachings with those of another reference).

... there is "a general rule that combination claims can consist of combinations of old elements as well as new elements," *Clearstream Wastewater Sys. v. Hydro-Action, Inc.*, 206 F.3d 1440, 1446, 54 USPQ2d 1185, 1189-90 (Fed. Cir. 2000), "[t]he notion . . . that combination claims can be declared invalid merely upon finding similar

elements in separate prior patents would necessarily destroy virtually all patents and cannot be the law under the statute, § 103." Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1575, 1 USPQ2d 1593, 1603 (Fed. Cir. 1987); Arkie Lures, Inc. v. Gene Larew Tackle, Inc., 119 F.3d 953, 957, 43 USPQ2d 1294, 1297 (Fed. Cir. 1997) ("It is insufficient to establish obviousness that the separate elements of the invention existed in the prior art, absent some teaching or suggestion, in the prior art, to combine the elements."). *Ruiz* at 1167

The motivation cited in the Office Action for the proposed combination is as follows:

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Lancaster et al's primers to Steinman method of PCR in order to detect different strains of HPV. Lancaster et al teach that HPV infection has high correlation with cervical cancer. It would have been prima facie obvious to combine Steinman method of strain differentiation with Lancaster et al's primers in order to detect the high risk strains HPV in patients.

Office Action at page 5, fifth paragraph. This statement does not provide the clear, particular suggestion in the art for making the specific claimed combination as is required under *In re Dembiczak*. The claims here are no more obvious than those at issue in *Dembiczak*. No clear, particular suggestion or motivation in the prior art to make the specific combination of “a plurality of primers substantially complementary to regions of both the nucleic acid from at least one selected strain of HPV and the nucleic acid from at least one non-selected strain of HPV” recited in claim 38 with “at least one probe [comprising a nucleic acid analog comprising PNA] that is sufficiently complementary to a portion of the nucleic acid from at least one non-selected strain to block full length amplification of the nucleic acid from at least one non-selected strain between the plurality of primers” and “amplifying said nucleic acid from at least one selected strain between said plurality of primers” also required by claim 38 has been provided, much less for the claims dependent thereon with their additional limitations. *Prima facie* obviousness has not been established under such conditions. Furthermore, Steinman and Orum cannot properly be combined. Steinman explicitly teaches away from the use of PNA blockers as used by Orum and recited in the claims. Lancaster teaches that his method is perfectly adequate for detecting different strains of HPV. The obviousness rejection is based on hindsight from these disparate references to provide random elements of the claims. There is no clear, particular motivation in the references to reach the claimed invention. Withdrawal of this rejection under 35 USC 103(a) is respectfully requested.

The rejection under 35 USC 103(a) over Steinman and Orum in view of Mahony

Claims 13, 15, 46 and 48 were rejected under 35 U.S.C. § 103(a) over Steinman and Orum in view of U.S. Patent No. 6,045,993 (“Mahony”). The rejection of claims 13 and 15 is rendered moot by their cancellation. The rejection of claims 46 and 48 is traversed.

Mahony describes the amplification of the L1 region from any of multiple strains of HPV using the MY09 and MY11 primers, and the subsequent use of a consensus sequencing primer to determine the positions of at least the A bases of any amplification product produced. See the abstract. Mahony does not teach or suggest the selective amplification of a particular strain of HPV, nor of any method available for doing so. Mahony teaches that his method is perfectly adequate for distinguishing which HPV strains are present in a sample.

The motivation cited in the Office Action for the proposed combination is as follows:

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Mahoney et al's primers to Steinman method of detection in order to amplify HPV in sample. Mahoney teach the successful amplification with SEQ IDNO:1 & 2 (see example 1). It would have been prima facie obvious to combine Mahoney et al's teachings of primers to Steinman in order to successfully amplify HPV for detection.

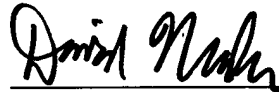
Office Action at page 6, second paragraph. Mahony adds no more clear, particular motivation to modify the references to reach the claimed invention than does Lancaster, and does not overcome this critical defect in the Steinman and Orum references. None of the cited references teach or suggest making the specific combination of "a plurality of primers substantially complementary to regions of both the nucleic acid from at least one selected strain of HPV and the nucleic acid from at least one non-selected strain of HPV" with "at least one probe [comprising a nucleic acid analog comprising PNA] that is sufficiently complementary to a portion of the nucleic acid from at least one non-selected strain to block full length amplification of the nucleic acid from at least one non-selected strain between the plurality of primers" and "amplifying said nucleic acid from at least one selected strain between said plurality of primers" required by these claims. Steinman and Orum cannot properly be combined, and Mahony teaches nonselective amplification and sequencing using universal primers as a proper method of distinguishing HPV strains. The combination of select elements from these references is based on hindsight in view of Applicants' disclosure. *Prima facie* obviousness of claims 46 and 48 has not been established. Withdrawal of this rejection under 35 USC 103(a) is respectfully requested.

**CONCLUSION**

Allowance of the claims is respectfully requested. The Examiner may call the Assignee's attorney at (650) 849-4908 to further advance prosecution of this case to issuance.

If the Commissioner determines that additional fees are due or that an excess fee has been paid, the Patent Office is authorized to debit or credit (respectively) Deposit Account No. 50-2518, reference no. 7030080000.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "David W. Maher", is written over a horizontal line.

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